UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/774,887	02/09/2004	Angel Lopez	029860-0154	8791

22428 7590 05/03/2007

FOLEY AND LARDNER LLP
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

EXAMINER	
MERTZ, PREMA MARIA	
ART UNIT	**PAPER NUMBER**
1646	

MAIL DATE	DELIVERY MODE
05/03/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/774,887	LOPEZ ET AL.	
	Examiner	Art Unit	
	Prema M. Mertz	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *27 March 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-35 and 40-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32-35, 40-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4)☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5)☐ Notice of Informal Patent Application
6)☐ Other: _____.

DETAILED ACTION

1. Amended claims 32, 33, 35 (3/27/07), previous claim 34, and new claims 40-43 (3/27/07) are pending and under consideration in the instant application.

2. Receipt of applicant's arguments filed on 3/27/2007 is acknowledged.

3. The following previous rejections and objections are withdrawn in light of applicants amendments filed on 3/27/2007:

(i) the objection to the title of the invention; and

(ii) the objection to claims 32-33 under 37 CFR 1.75 as being a substantial duplicate of claims 36-37.

4. Applicants arguments filed on 3/27/2007 have been fully considered but were non-persuasive. The issues remaining and new issues are stated below.

5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC 112, first paragraph, non-enablement

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6a. Claim 32-35, 40-43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for (i) a method of inhibiting IL-5, IL-3 or GM-CSF mediated leukaemic cell proliferation *in vitro* by contacting the leukaemic cells with monoclonal antibody BION-1 or fragments thereof capable of inhibiting the binding of cytokines lL-3, GM-

CSF and IL-5 to the common receptor βc, wherein the monoclonal antibody BION-1 or fragments thereof binds to both the B'-C' loop and the F'-G' of domain 4 of the βc subunit, and (ii) a method of inhibiting IL-5, IL-3 or GM-CSF mediated eosinophil activation, eosinophil production or eosinophil survival *in vitro*, by contacting the eosinophils with monoclonal antibody BION-1 or fragments thereof capable of inhibiting the binding of cytokines IL-3, GM-CSF and IL-5 to the common receptor βc, wherein the monoclonal antibody BION-1 or fragments thereof binds to both the B'-C' loop and the F'-G' of domain 4 of the βc subunit does not reasonably provide enablement for these methods *in vivo*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

This rejection is maintained for reasons of record set forth at pages 3-6 of the previous Office action of 9/27/2006.

Applicants argue that at the time of filing, it was known that leukemia involves activation of at least IL-3. However, contrary to Applicants arguments, other than the in vitro example on page 22, lines 11-17,

"BION-1 specifically inhibits chronic myelomonocytic cell growth

BION-1 is shown to inhibit the activity of one or all of IL-5, IL-3 & GM-CSF mediated effectors of leukaemic ceils. In particular BION-1 inhibits growth in vitro of chronic myelomonocytic cells (CMML), whereas a control antibody (IC1) does not (Figure 14). Furthermore, BION-I inhibits even in the presence of IL-3 whereas the control does not."

the specification fails to provide any guidance for the successful treatment of all leukemias with all monoclonal antibodies that inhibit binding of IL-3, GM-CSF or IL-5.

With respect to claims 32, 34, 40, 42, as recited, what is claimed in the instant invention broadly encompasses a method of administering "any and all" monoclonal antibodies that inhibit binding of IL-3, GM-CSF or IL-5 to achieve the claimed result. The specification is non-enabling for a method of administering these unlimited and unidentified monoclonal antibodies, which are encompassed by the scope of the claims. Claim 32, for example, is a single means claim (M.P.E.P. 2164.08(a)). In In re Hyatt, 708 F.2d 712, 218 USPQ 195 (Fed. Cir. 1983), the Courts have held that: A single means claim, i.e. where a means recitation does not appear in combination with another recited element of means, is subject to an undue breadth rejection under 35 U.S.C. 112, first paragraph. (A single means claim which covered every conceivable means for achieving the stated purpose was held nonenabling for the scope of the claim because the specification disclosed at most only those means known to the inventor). Since no material limitations for the monoclonal antibody have been recited in the claim and only a biological activity has been recited, the claim encompasses every conceivable structure (means) for achieving the stated property (result), a fact situation comparable to Hyatt. The claimed invention encompasses a method of administering compositions not envisioned or described in the specification, and neither does the specification disclose how these compositions can be distinguished from each other. The specification only enables a method of administering a BION-1 antibody having specific characteristics and properties. These properties differ structurally, chemically and physically from other known proteins. By application of the factors set forth in Ex parte Forman (230 USPQ 546 (Bd. Pat. App. & Int. 1986), and reiterated in In re Wands (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)), which include (1) quantity of experimentation, (2) guidance presented, (3) the predictability of the art, and (4) the breadth of

the claims, in the instant application, the quantity of experimentation to determine which antibodies are encompassed by the scope of the claims is practically infinite and the guidance provided in the specification very little, thereby rendering the results of the methods taught in the specification unpredictable (see pages 20-22). Therefore, it would require undue experimentation to determine which monoclonal antibodies having the desirable activity, would be encompassed by the scope of the method claims. The disclosure of using a single monoclonal antibody, BION-1, is clearly insufficient support under the first paragraph of 35 U.S.C. 112 for claims, which encompass a method of administering every and all monoclonal antibodies to these cytokines. In In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970), the Courts have held that: "Inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since some improvements while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; however, he must not be permitted to achieve this dominance by claims which are insufficiently supported and hence, not in compliance with first paragraph of 35 U.S.C. 112; that paragraph requires that the scope of the claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific law; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved."

Therefore, there are substantial scientific reasons to doubt the scope of enablement, as set forth above. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. The specification does not describe administering any other antibody polypeptides other than BION-1, and since it is deemed to constitute undue experimentation to determine all the others, the disclosure is not commensurate with the scope of the claims. It is suggested that by employing conventional claim language, the method claims be amended to recite the specific BION-1 antibody supported by the instant specification.

In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) states, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." "The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling" (MPEP 2164.03). The MPEP further states that physiological activity can be considered inherently unpredictable. Given the inherent unpredictability of physiological activity, which would include biological processes, i.e., methods of treatment, a certain amount of enablement beyond mere assertion must be required.

The method of instant claims 32-33 and 400-41 comprises the administration of a monoclonal antibody to treat leukemia. A first consideration would be the breadth of the claims.

The specification on page 22, lines 11-17, discloses that BION-1 inhibits growth of chronic myelomonocytic cells (CMML) in vitro. The Merck Manual (pages 944-955) teaches that there are different types of leukemias (malignant neoplasms of blood-forming tissues). There is acute lymphoblastic leukemia, acute myelogenous leukemia, chronic lymphocytic leukemia, chronic myelocytic leukemia, for which the usual treatments are myelosuppressive drugs but which treatments depend on the cell type involved. Remissions and survival tend to be brief in 20-25% of patients with myeloblastic transformation (see page 953, column 1, last paragraph). Therefore, the instant specification does not adequately teach how to effectively treat all these leukemias to reach a therapeutic endpoint by administering monoclonal antibody compositions as recited in the claims. The Merck Manual indicates that absent any data, it would require undue experimentation to practice the claimed method of treatment of all malignant neoplasms of blood-forming tissues.

The CAFC decision (Genentech Inc. v. Novo Nordisk, 42 USPQ2d 1001, 1997) expressly states that:

"When there is no disclosure of any specific starting material or of any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement".

In the instant case, the limited results presented for in vitro CMML, is not sufficient to enable the breadth of the claims and are not predictive of in vivo efficacy for treatment of all

blood-forming tissue malignancies. The treatment of malignancies has been the subject of intense study for the past several decades. Many promising treatments and therapies have been identified via in vitro experiments, and have not lived up to expectations when tested in vivo. In fact, the number of such treatments, which have failed to live up to their promise exceeds those, which have been performed as hoped by orders of magnitude. The disclosure fails to teach one of ordinary skill in the art a method treatment against all leukemias. The effectivity of the claimed method against one type of leukemia is different from another specific type of leukemia depending on the type of blood cells involved and the developmental stage of the malignancy. The skilled artisan would have to undergo undue experimentation to determine if there is an effective amount of the antibody to be utilized against the various types of leukemias. It would not be reasonable to expect the antibodies to work on the various types of aforementioned leukemias because of the different types of blood cell types involved. Thus, it would require undue experimentation on the part of the skilled artisan to use the claimed method for treated as recited, in the absence of sufficient information to predict the results with an adequate degree of certainty. In view of this unpredictability in the treatment of different leukemias, there cannot be said to be any reasonable expectation of success at the in vivo application of a potential therapy, especially in view of the fact that the current specification as filed presents no working examples pertaining to the method of treatment of various leukemias in vivo. The recitation of "leukemic cell" in claim 32, for example, is not commensurate with the scope of the specification. Given the breadth of claim 32 in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant

specification and the prior art of record, it would require undue experimentation for one of skill in the art to practice the claimed invention.

Claim Rejections - 35 USC § 112, second paragraph

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 32-35, 40-43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

This rejection is maintained for reasons of record set forth at pages 6-7 of the previous Office action of 9/27/2006.

Claims 32-35, 40-43 are rejected as incomplete because the claims fail to recite method steps. Applicants argue that the claims are not incomplete and do recite method steps because the claims recite the active step of "contacting" the cells with the antibody. However, contrary to Applicants arguments, the claims fail to recite (i) that the antibody is effective to treat a condition; and (ii) a results step. Therefore, this rejection is being maintained for reasons of record.

Conclusion

No claims are allowed.

Claims 32-35, 40-43 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (571) 272-0876. The examiner can normally be reached on Monday-Friday from 7:00AM to 3:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835.

Official papers filed by fax should be directed to (571) 273-8300. Faxed draft or informal communications with the examiner should be directed to (571) 273-0876.

Information regarding the status of an application may be obtained from the Patent application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Prema Mertz

Prema Mertz Ph.D., J.D.
Primary Examiner

Art Unit 1646
April 16, 2007